Bioscience Hypotheses (2009) 2, 417—421

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/bihy

Pulmonary artery calcification in racehorses may be related to transient and repeated increases in arterial pressure during exercise

Matthew G. Teeter [a], Luis G. Arroyo [b,*], Jeremy D. Bakker [a], R. John Runciman [a], Laurent Viel [b]

[a] School of Engineering, University of Guelph, Ontario, Canada N1G 2W1
[b] Department of Clinical Studies, University of Guelph, 50 Stone Road E, Guelph, Ontario, Canada N1G 2W1

Received 24 June 2009; received in revised form 29 July 2009; accepted 31 July 2009

KEYWORDS
Arterial calcification;
Horses;
Pulmonary artery;
Exercise;
Pulmonary hypertension

Abstract Calcification of the pulmonary artery has been found in a large number of racing horses. The majority of calcified lesions are found immediately distal to the primary arterial bifurcation. Increased arterial wall stress levels have been previously demonstrated at these locations, with the wall stress levels increasing under intra-luminal pressures associated with exercise. We hypothesize therefore that the formation of calcified lesions is mediated by transient and repeated increases in pulmonary artery intra-luminal pressure. The presence of calcified lesions would likely further exacerbate the levels of wall stress, leading to growth of the lesions. A level of wall stress may exist above which calcified lesions form, and a second level may exist above which the calcified lesions grow at an increased rate. A computer model of pulmonary artery wall stress with calcified lesions was created, and wall stress levels were found to be greatest at the periphery of the calcified lesions. Osteo/chondrocyte-like cells have also been found at the periphery of the calcified lesions and could be responsible for collagen deposition and lesion growth, mediated by local wall stress levels. These increased levels of wall stress could place racehorses at a greater risk of acute pulmonary arterial rupture at the site of the calcified lesions, due to the high levels of intra-luminal pressure within the pulmonary artery during exercise. The hypothesis may also have implications in the etiology of human vascular diseases.
© 2009 Elsevier Ltd. All rights reserved.

Introduction

Arterial calcification in horses is characterized by the deposition of calcium within the tunica media of the vascular wall [1,2]. It has been shown in humans that the presence of calcified lesions leads to stiffening of the

* Corresponding author. Tel.: +1 519 824 4120.
E-mail address: larroyo@uoguelph.ca (L.G. Arroyo).

1756-2392/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bihy.2009.07.011

vasculature, decreasing the compliance of the vessels and therefore decreasing their adaptability to changes in blood pressure [3]. Arterial calcification has been the subject of a number of investigations in human subjects, but much remains to be learned regarding its pathogenesis [3,4].

Lesions have been found in the aorta, pulmonary artery, and carotid arteries of horses [1,2,5]. In the study of Arroyo et al. [2] the pulmonary artery was preferentially affected, with lesions appearing in the pulmonary artery branches in 82% of racehorse cases compared to 16% in aortic trunks and 15% in carotid trunks. The pulmonary artery trunk was also affected in 31% of cases [2]. In the studies of Cranley [1] and Arroyo et al. [2] the majority of lesions within the pulmonary artery were found immediately distal to and involving part or the entire circumference of the primary artery bifurcation.

Hypothesis

We have previously demonstrated (using computer modeling) increased arterial wall stress levels at the sites within the equine pulmonary artery where calcified lesions form, with the wall stress levels increasing under intra-luminal pressures associated with exercise [6]. As these calcified lesions are apparently more prevalent in racehorses [1,2,5], we therefore postulate that the formation of calcified lesions is due, at least in part, to arterial wall stress from transient and repeated increases in intra-luminal arterial pressure during exercise. Because the presence of calcified lesions leads to increased vascular stiffness and decreased compliance [3], wall stress would likely be increased within the lesions. This would further exacerbate the calcification—stress interaction, and may potentially be the cause of localized lesion growth. A level of stress may exist above which lesions form, and a second level may exist above which lesions grow at an increased rate. The stress level required for lesion formation is likely associated with increased intra-luminal pressure within the pulmonary artery.

If true, racehorses would therefore be at a greater risk of arterial wall injuries and/or rupture as they experience transient pulmonary arterial hypertension during exercise [7], creating increased wall stress levels. This is particularly concerning as it appears that racehorses may be more susceptible to arterial calcification [1,2,5]. There is currently limited information regarding the consequences of arterial calcification in horses. Sudden death of horses from rupture of the pulmonary artery and dissecting aortic aneurysm has been reported [8,9]. In both of these cases, degenerative changes and calcification were found within the tunica media of the affected arteries [8,9].

Simulation of wall stress within calcified lesions of the pulmonary artery

To test the hypothesis that increased arterial wall stress levels would be located within calcified lesions a finite element analysis (FEA) approach was utilized. Two solid models of the equine pulmonary artery were taken from our previous study examining arterial wall stress in healthy horses [6]. Using SolidWorks (2007 Version, SolidWorks Inc., Concord, MA) artificial calcified lesions were created within the wall of the left and right branches of the artery model (Fig. 1), approximately 10 mm distal and ipsilateral to the bifurcation. Mild, moderate and severe lesion sizes were created based on the grading criteria of Arroyo et al. (2008), and were formed as simple extruded shapes with rounded edges in the model.

Mild was set as a 10-mm diameter circle and moderate as a 25 mm by 10 mm rectangle with 5 mm radius corners. Severe was the same shape as moderate but extending 50% of the way around the artery. New models with a single mild, moderate, or severe lesion were created from each of the two base models, for a total of 12-modeled lesions. Stress values within the normal artery wall and lesion were modeled by assuming homogeneous material properties. Hydrostatic pressure of 100 mmHg for each analysis was applied to the entire inner surface, which corresponds to mean systolic exercising pressure in the pulmonary artery of horses [7]. The artery was assumed to be isotropic and incompressible, with a Poisson's ratio of 0.45, as used in other studies [10]. A modulus of 260 kPa from the human pulmonary artery was used [11], as the elastic modulus of the equine pulmonary artery has not been determined. The material properties for the lesions were based on abdominal aortic calcification, which has a Poisson's ratio of 0.45 and an elastic modulus of 1.47 MPa [12]. Boundary conditions were applied at the trunk and bifurcation openings and the FEA was performed.

For each model the peak wall stress was recorded at the circumferential and axial edges of the lesions as well as at the lesion centre. Mean wall stress values at these locations were calculated for the mild, moderate and severe lesions sizes. The nominal level of wall stress in the region where lesions were placed in each of the base models was also recorded.

High levels of wall stress were consistently found at the site of the modeled lesions (Fig. 2). All stress levels were higher within the lesions than in the wall surrounding the lesions (Table 1), and higher than the nominal stress level (108 ± 20 kPa) in the normal wall before the lesions were added to the model. The stress levels within the lesions were highest at the circumferential edge of the lesions, followed by the axial edge, and lowest at the centre of the lesion.

Discussion

The study described here suggests that arterial wall stress levels are increased within calcified lesions in the equine pulmonary artery. The magnitude of these stresses increases with the severity of the lesion such that wall stress within the most severe lesions is greater than anywhere else in the arterial wall. Within the lesions themselves, stress is highest at the circumferential edge, lower but still high at the axial edge, and the lowest at the lesion centre. All points within the lesions have higher stress levels than the nominal stress in the wall without a lesion.

Clinically, lesions range in macroscopic size from mild plaques of approximately 5 mm diameter to severe, extensive patches involving the whole circumference of the arterial wall [2]. Many osteo/chondrocyte-like cells have been found around the periphery of moderately and severely calcified lesions [1,2]. It has been hypothesized that these cells may be responsible for synthesis of

Download English Version:

https://daneshyari.com/en/article/2034776

Download Persian Version:

https://daneshyari.com/article/2034776

Daneshyari.com